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PTO-1590 (8-01)

11902

Delaval, Jan

From: Huynh, Phuong N.
Sent: Wednesday, April 21, 2004 8:44 AM
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Subject: RE: 10/005,907

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Please search polynucleotide encoding the amino acid sequence of SEQ ID NO: 2 (open),
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=> s l1 and mast cell
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L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2003:282747 Document No. 138:298936 Human **genes** differentially expressed in **mast cells** and their association with **mast cell** activation. **Nocka, Karl**; Medley, Quintus; Thomis, Daniel; Gu, Jessie; Lu, Sun (Ucb, S.A., Belg.). PCT Int. Appl. WO 2003029464 A2 20030410, 120 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-EP10897 20020927. PRIORITY: US 2001-PV325536 20011001.
AB The invention relates generally to the changes in **gene** expression in **mast cells** and tissues removed from patients with allergic hypersensitivity. The invention specifically relates to the **genes** MC21, MC22, MC25, MC33, MC36, and MC39, which are differentially expressed in **mast cells** compared to normal tissues and in resting **mast cells** vs. activated **mast cells.**

L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
2002:449849 Document No. 137:32077 Allergic hypersensitivity-associated **genes** and proteins for diagnosis and treatment of rhinitis, atopic dermatitis, urticaria, asthma and mastocytosis. **Nocka, Karl; Pirozzi, Gregory; Einstein, Richard** (UCB, S.A., Belg.). PCT Int. Appl. WO 2002046389 A2 20020613, 119 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE,

SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46180 20011207. PRIORITY: US 2000-PV251835 20001208; US 2001-PV275479 20010314; US 2001-PV279115 20010328; US 2001-PV280143 20010402.

AB The invention relates generally to the changes in **gene** expression in **mast cells** during maturation and in tissues removed from patients with urticaria or allergic hypersensitivity relative to **gene** expression in **mast cells** removed from normal subjects. The invention specifically relates to four novel **gene** families which are differentially expressed in **mast cells** and allergic hypersensitivity diseases, such as urticaria, compared to normal tissues. The **genes** and protein products are useful for diagnosis and treatment of seasonal rhinitis, atopic dermatitis, urticaria, asthma, mastocytosis, and allergic hypersensitivity. The **genes** and proteins are also useful for identifying agonists and antagonists for therapeutic use.

L4 ANSWER 3 OF 17 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 1

97349208 EMBASE Document No.: 1997349208. Increased growth promoting but not **mast cell** degranulation potential of a covalent dimer of c-kit ligand. **Nocka K.H.**; Levine B.A.; Ko J.-L.; Burch P.M.; Landgraf B.E.; Segal R.; Lobell R.. Dr. K.H. Nocka, CytoMed Inc, 840 Memorial Dr, Cambridge, MA 02139, United States. Blood 90/10 (3874-3883) 1997.

Refs: 53.

ISSN: 0006-4971. CODEN: BLOOAW. Pub. Country: United States. Language: English. Summary Language: English.

AB The native form of soluble c-kit ligand (KL) is a noncovalent dimer. We have isolated a soluble, disulfide-linked dimer of murine KL (KL-CD) by expressing KL in Escherichia coli and refolding the denatured protein under conditions that promote the formation of both noncovalent dimers (KL-NC) and KL-CD. KL-CD exhibits a 10- to 15-fold increase in the ability to stimulate the growth of both the human megakaryocytic cell line MO7e and murine bone marrow-derived **mast cells** relative to KL-NC. Colony-forming assays of murine bone marrow progenitor cells also reflected this increased potency. However, KL-CD and KL-NC are equally able to prime **mast cells** for enhanced IgE- dependent degranulation in vitro and activate **mast cells** in vivo. Improving the growth-promoting activity of KL without changing its **mast cell** activation potential suggests that KL-CD or a related molecule could be administered in the clinic at doses that stimulate hematopoietic recovery while avoiding significant **mast cell** activation.

L4 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 2

96437052. PubMed ID: 8839868. Targeted disruption of guanosine diphosphate-dissociation inhibitor for Rho-related proteins, GDID4: normal hematopoietic differentiation but subtle defect in superoxide production by macrophages derived from in vitro embryonal stem cell differentiation. Guillemot J C; Kruskal B A; Adra C N; Zhu S; Ko J L; Burch P; **Nocka K**; Seetoo K; Simons E; Lim B. (Division of Hematology/Oncology, Beth Israel Hospital, Harvard Medical School, Boston, MA, USA.) Blood, (1996 Oct 1) 88 (7) 2722-31. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB The Rho subfamily of small guanosine triphosphate (GTP)-binding proteins, through their role in cytoskeletal organization, is involved in diverse cellular functions, including cell motility and morphologic changes during differentiation. Rac also has a special role in the production of superoxide, a key component in phagocytic antimicrobial function. Guanosine diphosphate (GDP)-dissociation inhibitors (GDIs) belong to one of three classes of proteins that regulate the critical cycling of GTP-binding proteins between the inactive and active states. Two homologous GDIs for the Rho subfamily have been identified. GDID4 is

preferentially expressed in hematopoietic cells, while RhoGDI is ubiquitously expressed. Whether different physiologic functions are subserved by the two GDIs is unknown. We have derived embryonal stem (ES) cells with targeted disruption of both alleles of the GDID4 **gene** and examined hematopoiesis and phagocytic functions of macrophages derived from in vitro ES-cell differentiation. GDID4-/- ES cells develop like wild-type cells into colonies that contain heterogeneous populations of progenitor cells and differentiated erythromyeloid cells. GDID4-/- cells express no GDID4 protein, but have normal levels of RhoGDI. GDID4-/- macrophages phagocytose yeasts and antibody-opsonized erythrocytes as effectively as wild-type macrophages. However, a slight but consistent reduction in their capacity to generate superoxide was observed, which suggests new insight into the cellular role of GDID4. The minimal phenotypic effect of a loss of function of GDID4 also indicates a significant redundancy of function between GDID4 and RhoGDI. Their functional repertoire may be better revealed by a disruption of both **genes**. The use of hematopoietic cells derived in vitro from genotypically altered ES cells avoids the difficulties inherent in generating knockout animals and is a useful complementary approach for evaluating the **gene** function.

L4 ANSWER 5 OF 17 MEDLINE on STN DUPLICATE 3
96094478. PubMed ID: 7499870. Identification and characterization of a novel surface antigen **gene** induced in **mast cells** activated through the high affinity IgE receptor.
Pirozzi G; Terry R W; Epstein D; Labow M A. (Cytogen Corp., Princeton, NJ 08540, USA.) Journal of immunology (Baltimore, Md. : 1950), (1995 Dec 15) 155 (12) 5811-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB In an effort to isolate novel **genes** involved in inflammation and/or **mast cell** activation, we have used a combination of differential screening and subtractive hybridization to isolate **genes** whose expression are induced upon activation of a transformed rat **mast cell** line. One of the isolated clones, pMCA-32, contained an open reading frame of 278 amino acids that included a putative hydrophobic transmembrane domain, a cysteine rich Ig-like extracellular domain, and a cytoplasmic domain containing three consensus SH2-domain phosphotyrosine binding sites. The MCA-32 **gene** is also highly conserved between rat and mouse, with the two coding regions being 73% identical. Although the MCA-32 coding region did not contain an obvious signal peptide, MCA-32 protein was detected on the surface of rat **mast cells**, and the cloned cDNA produced a cell surface protein when expressed in COS-7 cells. MCA-32 RNA from both mouse and rat undergoes alternative splicing, producing an mRNA containing an in-frame deletion of the TM domain, suggesting that a form of MCA-32 protein may be secreted. MCA-32 mRNA expression was up-regulated upon activation of RBL-2H3 cells and was highly abundant in primary peritoneal **mast cells**. Expression of MCA-32 RNA was only observed in primary and transformed **mast cells** from rat, while in the mouse MCA-32, RNA was also produced in significant amounts by a number of transformed monocyte cell lines. Thus, MCA-32 is a novel surface protein whose structure and expression suggest roles in the development and/or activation of **mast cells** and monocytes.

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1994:97212 Document No. 120:97212 Ligand for the c-kit receptor and methods of use thereof. Besmer, Peter; Buck, Jochen; Moore, Malcolm A. S.; **Nocka, Karl** (Sloan-Kettering Institute for Cancer Research, USA). PCT Int. Appl. WO 9321936 A1 19931111, 215 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US3640 19930416. PRIORITY: US 1992-873962 19920423.

AB A pharmaceutical composition which comprises purified or recombinant c-kit ligand (KL) in combination with other hematopoietic factors and a pharmaceutically acceptable carrier is provided as well as methods of treating patients which comprise administering to the patient the pharmaceutical composition of this invention. This invention provides combination therapies using KL and a KL polypeptide, or a soluble fragment thereof and other hematopoietic factors. It also provides methods and compns. for ex-vivo use of KL alone or in combination therapy. A mutated KL antagonist is also described. Such an antagonist may also be a small mol. Antisense nucleic acids to KL as therapeutics are also described. Lastly, compns. and methods are described that take advantage of the role of KL in germ cells, **mast cells** and melanocytes. KL was purified from mouse fibroblast conditioned medium and cDNA was isolated and sequenced. The interactions of IL-1, IL-6, and KL on primitive murine progenitor cell compartments were studied. There were synergistic and additive effects of these factors alone or in conjunction with CSFs. IL-1, IL-6, and KL stimulate early hematopoiesis.

L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1992:585617 Document No. 117:185617 A protein binding the receptor for the c-kit **gene** product for therapeutic uses. Besmer, Peter; **Nocka, Karl**; Buck, Jochen; Moore, Malcolm A. S. (Sloan-Kettering Institute for Cancer Research, USA). PCT Int. Appl. WO 9203459 A1 19920305, 146 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, SU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US6130 19910827. PRIORITY: US 1990-573483 19900827; US 1990-594306 19901005.

AB A heterodimeric protein that specifically binds the c-kit receptor (kit ligand, KL) is purified from mouse and cDNAs encoding the subunits are cloned and expressed in animal cells. The protein stimulates erythroid differentiation and is useful for treatment of leucopenia (no data). The protein was purified chromatog. from conditioned medium from mouse fibroblast cultures using a **mast cell** proliferation assay to detect the activity. The assay used W/WV **mast cells** as a neg. control; it was found that responses of cells carrying mutant alleles at the W locus correlated with the physiol. severity of the phenotype. In vitro the protein stimulated BFU-E erythroid bursts in fetal liver and spleen cells in a dose-dependent manner when used in combination with erythropoietin; it was not effective on bone marrow cells. A cDNA was cloned by reverse transcription-polymerase chain reaction using amino acid sequence-derived oligonucleotide primers. The **gene** mapped very near the Sl locus (0.8 cM). Soluble and membrane-bound forms of the protein arise by differential splicing of the mRNA precursor with the splicing tissue-specifically controlled.

L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1993:207768 Document No. 118:207768 Differential expression and processing of two cell associated forms of the Kit-ligand: KL-1 and KL-2. Huang, Eric J.; **Nocka, Karl H.**; Buck, Jochen; Besmer, Peter (Programs Mol. Biol., Sloan Kettering Inst., New York, NY, 10021, USA). Molecular Biology of the Cell, 3(3), 349-62 (English) 1992. CODEN: MBCEEV. ISSN: 1059-1524.

AB The c-kit ligand, KL, and its receptor, the proto-oncogene c-kit are encoded, resp., at the steel (Sl) and white spotting (W) loci of the mouse. Both Sl and W mutations affect cellular targets in melanogenesis, gametogenesis, and hematopoiesis during development and in adult life. Although identified as a soluble protein, the predicted amino acid sequence of KL indicates that it is an integral transmembrane protein. The authors have investigated the relationship between the soluble and the cell associated forms of KL and the regulation of their expression. The soluble form of KL is generated by efficient proteolytic cleavage from a transmembrane precursor, KL-1. An alternatively spliced version of KL-1, KL-2, in which

the major proteolytic cleavage site is removed by splicing, is shown to produce a soluble biol. active form of KL as well, although with somewhat diminished efficiency. The protein kinase C inducer phorbol 12-myristate 13-acetate and the calcium ionophore A23187 were shown to induce the cleavage of both KL-1 and KL-2 at similar rates, suggesting that this process can be regulated differentially. Furthermore, proteolytic processing of both the KL-1 and KL-2 transmembrane protein products was shown to occur on the cell surface. The relative abundance of KL-1 and KL-2 in a wide variety of different mouse tissues indicates that the expression of KL-1 and KL-2 is controlled in a tissue-specific manner. Sld, a viable steel allele, is shown to encode a biol. active secreted mutant KL protein. These results indicate an important function for both the soluble and the cell associate form of KL. The resp. roles of the soluble and
cell associated forms of KL in the proliferative and migratory functions of c-kit are discussed.

L4 ANSWER 9 OF 17 MEDLINE on STN DUPLICATE 4
91208397. PubMed ID: 1708291. Monoclonal antibody YB5.B8 identifies the human c-kit protein product. Lerner N B; **Nocka K H**; Cole S R; Qiu F H; Strife A; Ashman L K; Besmer P. (Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY.) Blood, (1991 May 1) 77 (9) 1876-83. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB The c-kit proto-oncogene encodes a 145- to 160-Kd transmembrane tyrosine kinase, which is a member of the platelet-derived growth factor receptor family and is allelic with the murine white spotting locus (W). W mutations affect several aspects of hematopoiesis, most notably erythroid progenitors and **mast cells**. A monoclonal antibody, YB5.B8, had been raised against the leukemic blasts of a patient with M1-type acute myelocytic leukemia (AML) and it precipitates a 150-Kd cell surface glycoprotein from leukemic cells. The YB5.B8 epitope is expressed on **mast cells**, on up to 3% of normal mononuclear bone marrow cells, and it identifies a sub-group of AML patients with a poor prognosis. In view of similarities noted between the cell surface antigen identified by YB5.B8 and the c-kit protein product, we performed experiments to determine whether they are identical. c-kit RNA expression in the cell lines HEL (human erythroleukemia) and A172 (glioblastoma) was shown to parallel the expression of the YB5.B8 epitope in these lines as measured by flow cytometry. Immunoprecipitation analysis with anti-kit serum and YB5.B8 antibody indicated that the two antibodies identified proteins of identical size in HEL (155 Kd) and A172 (145 Kd) cells, and sequential immunoprecipitations with the kit and the YB5.B8 antibodies demonstrated that the two antibodies recognize the same molecule. The proteins identified by both the anti-kit and YB5.B8 antibodies displayed in vitro autophosphorylation activity in immune complex kinase assays. In addition, YB5.B8 was able to inhibit the binding of the kit ligand to HEL cells. These studies provide evidence that the YB5.B8 antigen and the c-kit protein product are identical and raise certain hypotheses regarding the role of c-kit in AML.

L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1991:75730 Document No. 114:75730 Candidate ligand for the c-kit transmembrane kinase receptor: KL, a fibroblast derived growth factor stimulates **mast cells** and erythroid progenitors.
Nocka, Karl; Buck, Jochen; Levi, Ester; Besmer, Peter (Grad. Sch. Med. Sci., Cornell Univ., New York, NY, 10021, USA). EMBO Journal, 9(10), 3287-94 (English) 1990. CODEN: EMJODG. ISSN: 0261-4189.

AB A **mast cell** proliferation assay was used to purify a 30-kd protein, designated KL, from conditioned medium of Balb/3T3 fibroblasts to apparent homogeneity. KL stimulates the proliferation of normal bone marrow-derived **mast cells** but not **mast cells** from W (white-spotting locus) mice, although

both normal and mutant **mast cells** respond similarly to interleukin-3. Connective tissue-type **mast cells** derived from the peritoneal cavity of normal mice were found to express a high level of c-kit protein on their surface and to proliferate in response to KL. The effect of KL on erythroid progenitor cells was investigated as well. In combination with erythropoietin, KL stimulated early erythroid progenitors (BFU-E) from fetal liver and spleen cells but not from bone marrow cells of adult mice or from fetal liver cells of W/W mice. Taken together, the biol. properties of KL are in agreement with those expected of the ligand of c-kit with regard to **mast cell** biol. and aspects of erythropoiesis, and therefore, KL may be the ligand of the c-kit receptor.

L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
1990:510275 Document No. 113:110275 Molecular bases of dominant negative and loss of function mutations at the murine c-kit/white spotting locus: W37, Wv, W41 and W. **Nocka, Karl**; Tan, Jimmy C.; Chiu, Easter; Chu, Tang Y.; Ray, Prabir; Traktman, Paula; Besmer, Peter (Mol. Biol. Program, Sloan Kettering Inst., New York, NY, 10021, USA). EMBO Journal, 9(6), 1805-13 (English) 1990. CODEN: EMJODG. ISSN: 0261-4189.

AB The proto-oncogene c-kit encodes a transmembrane tyrosine protein kinase receptor for an unknown ligand and is allelic with the murine white -spotting locus (W). Mutations at the W locus affect various aspects of hematopoiesis, the proliferation and migration of primordial germ cells and melanoblasts during development. The original W mutation and W37 are severe lethal mutations when homozygous. In the heterozygous state, the W mutation has a weak phenotype whereas W37 has dominant characteristics. Wv And W41 are weak W mutations with dominant characteristics. The mol. basis of these 4 W mutations and their effects on **mast cell** differentiation were characterized by using a fibroblast/ **mast cell** co-culture assay. W37, Wv, And W41 are the result of missense mutations in the kinase domain of the c-kit coding sequence (37 E → K at position 582; Wv T → M position 660 and W41 V → M position 831), which affect the c-kit associated tyrosine kinase to varing degrees. The c-kit products in homozygous mutant **mast cells** are expressed normally, although the 160 kDa cell membrane form of the c-kitW37 protein displays accelerated turnover characteristics. The W mutation is the result of a 78-amino-acid deletion which includes the transmembrane domain of the c-kit protein. A 125-kDa c-kit protein was detected in homozygous W/W **mast cells** which lacks kinase activity and is not expressed on the cell surface. These results provide an explanation for the dominant nature of the W37, Wv, and W41 mutations and for the null phenotype of the original W mutation, and they also provide insight into the mechanism of c-kit-mediated signal transduction.

L4 ANSWER 12 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
91:19996 The Genuine Article (R) Number: EQ223. GONADAL EXPRESSION OF C-KIT ENCODED AT THE W-LOCUS OF THE MOUSE. MANOVA K; **NOCKA K**; BESMER P; BACHVAROVA R F (Reprint). CORNELL UNIV, MED CTR, COLL MED, DEPT CELL BIOL & ANAT, NEW YORK, NY, 10021; SLOAN KETTERING MEM CANC CTR, MOLEC BIOL PROGRAM, NEW YORK, NY, 10021; CORNELL UNIV, GRAD SCH MED SCI, NEW YORK, NY, 10021. DEVELOPMENT (1990) Vol. 110, No. 4, pp. 1057-1069. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recently, it has been shown that the c-kit proto-oncogene is encoded at the white spotting (W) locus in mice. Mutations of this **gene** cause depletion of germ cells, some hematopoietic cells and melanocytes. In order to define further the role of c-kit in gametogenesis, we have examined its expression in late fetal and postnatal ovaries and in postnatal testis. By RNA blot analysis, c-kit transcripts were not detected in late fetal ovaries but appeared at birth. The relative amount reached a maximum in ovaries of juvenile mice, and decreased in adult

ovaries. c-kit transcripts were present in increasing amounts in isolated primordial, growing and full-grown oocytes, as well as in ovulated eggs. Little was detected in early 2-cell embryos and none in blastocysts. In situ hybridization revealed c-kit transcripts in a few oocytes of late fetal ovaries and in all oocytes (from primordial to full-grown) in ovaries from juvenile and adult mice. Expression was also observed in ovarian interstitial tissue from 14 days of age onward. Using indirect immunofluorescence, the c-kit protein was detected on the surface of primordial, growing and full-grown oocytes, as well as on embryos at the 1- and 2-cell stages; little remained in blastocysts.

In situ hybridization analysis of testes from mice of different ages demonstrated expression in spermatogonia from 6 days of age onward. Using information provided by determining the stage of the cycle of the seminiferous epithelium for a given tubule and by following the age dependence of labeling, it was concluded that the period of expression of c-kit extends from at least as early at type A2 spermatogonia through type B spermatogonia and into preleptotene spermatocytes. Leydig cells were labelled at all ages examined.

The expression pattern in oocytes correlates most strongly with oocyte growth and in male germ cells with gonial proliferation.

L4 ANSWER 13 OF 17 MEDLINE on STN DUPLICATE 5

91004221. PubMed ID: 1698557. The hematopoietic growth factor KL is encoded by the Sl locus and is the ligand of the c-kit receptor, the **gene** product of the W locus. Huang E; **Nocka K**; Beier D R; Chu T Y; Buck J; Lahm H W; Wellner D; Leder P; Besmer P. (Molecular Biology Program, Sloan Kettering Institute, New York, New York.) Cell, (1990 Oct 5) 63 (1) 225-33. Journal code: 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB Mutations at the steel locus (Sl) of the mouse affect the same cellular targets as mutations at the white spotting locus (W), which is allelic with the c-kit proto-oncogene. We show that KL, a hematopoietic growth factor obtained from conditioned medium of BALB/c 3T3 fibroblasts that stimulates the proliferation of **mast cells** and early erythroid progenitors, specifically binds to the c-kit receptor. The predicted amino acid sequence of isolated KL-specific cDNA clones suggests that KL is synthesized as an integral transmembrane protein. Linkage analysis maps the KL **gene** to the Sl locus on mouse chromosome 10, and KL sequences are deleted in the genome of the Sl mouse. These results indicate that the Sl locus encodes the ligand of the c-kit receptor, KL.

L4 ANSWER 14 OF 17 MEDLINE on STN DUPLICATE 6

90100577. PubMed ID: 1688471. The dominant W42 spotting phenotype results from a missense mutation in the c-kit receptor kinase. Tan J C; **Nocka K**; Ray P; Traktman P; Besmer P. (Molecular Biology Program, Sloan Kettering Institute, New York, NY 10021.) Science, (1990 Jan 12) 247 (4939) 209-12. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB The murine white spotting locus (W) is allelic with the proto-oncogene c-kit, which encodes a transmembrane tyrosine protein kinase receptor for an unknown ligand. Mutations at the W locus affect various aspects of hematopoiesis and the proliferation and migration of primordial germ cells and melanoblasts during development to varying degrees of severity. The W42 mutation has a particularly severe effect in both the homozygous and the heterozygous states. The molecular basis of the W42 mutation was determined. The c-kit protein products in homozygous mutant **mast cells** were expressed normally but displayed a defective tyrosine kinase activity in vitro. Nucleotide sequence analysis of mutant complementary DNAs revealed a missense mutation that replaces aspartic acid with asparagine at position 790 in the c-kit protein product. Aspartic acid-790 is a conserved residue in all protein kinases. These results provide an explanation for the dominant nature of the W42 mutation

and provide insight into the mechanism of c-kit-mediated signal transduction.

L4 ANSWER 15 OF 17 MEDLINE on STN DUPLICATE 7

90200630. PubMed ID: 1690623. The mouse W/c-kit locus. Bernstein A; Chabot B; Dubreuil P; Reith A; **Nocka K**; Majumder S; Ray P; Besmer P. (Division of Molecular and Developmental Biology, Mt. Sinai Hospital Research Institute, Toronto, Ontario, Canada.) Ciba Foundation symposium, (1990) 148 158-66; discussion 166-72. Ref: 19. Journal code: 0356636. ISSN: 0300-5208. Pub. country: Netherlands. Language: English.

AB The mature cells in the haemopoietic system arise as the result of the extensive developmental and proliferative capacity of pluripotential stem cells. In order to understand the molecular basis for these developmental processes, it will be necessary to identify and characterize the cellular **genes** that control early steps in haemopoiesis. Mutations at the mouse W locus on chromosome 5 lead to pleiotropic developmental defects, including sterility, coat colour abnormalities, severe macrocytic anaemia and **mast cell** deficiency. The defects in all these lineages are cell autonomous and intrinsic, suggesting that the W locus encodes a **gene** product required directly for cellular differentiation. In an attempt to understand this classical mouse developmental mutation, we have demonstrated that the c-kit proto-oncogene, which encodes a transmembrane receptor tyrosine kinase, is very closely linked to W. Several further observations are consistent with the idea that W and c-kit are allelic: first, c-kit is expressed in those cell populations affected by W mutations; second, the expression of c-kit transcripts can be affected by mutations at the W locus; third, the tyrosine kinase activity associated with the protein encoded by c-kit is functionally impaired in **mast cells** derived from mutant W/Wv mice; and fourth, rearrangements within the c-kit **gene** have been reported in two W mutant alleles. These observations suggest that the dominant phenotype associated with W mutations results from loss-of-function alterations that affect the receptor tyrosine kinase encoded by c-kit. The demonstration that the W locus encodes a transmembrane growth factor receptor provides a molecular basis for understanding the intrinsic haemopoietic defect in W mutant mice and the role that this cellular proto-oncogene plays in haemopoiesis and other developmental processes.

L4 ANSWER 16 OF 17 MEDLINE on STN DUPLICATE 8

89306618. PubMed ID: 2473008. Expression of c-kit **gene** products in known cellular targets of W mutations in normal and W mutant mice--evidence for an impaired c-kit kinase in mutant mice. **Nocka K**; Majumder S; Chabot B; Ray P; Cervone M; Bernstein A; Besmer P. (Molecular Biology Program, Sloan Kettering Institute, New York, New York.) Genes & development, (1989 Jun) 3 (6) 816-26. Journal code: 8711660. ISSN: 0890-9369. Pub. country: United States. Language: English.

AB The proto-oncogene c-kit, a transmembrane tyrosine protein kinase receptor for an unknown ligand, was shown recently to map to the dominant white spotting locus (W) of the mouse. Mutations at the W locus affect various aspects of hematopoiesis, as well as the proliferation and/or migration of primordial germ cells and melanoblasts during development. Here, we show that c-kit is expressed in tissues known to be affected by W mutations in fetal and adult erythropoietic tissues, **mast cells**, and neural-crest-derived melanocytes. We demonstrate that the c-kit associated tyrosine-specific protein kinase is functionally impaired in W/WV **mast cells**, thus providing a molecular basis for understanding the developmental defects that result from these mutations.

L4 ANSWER 17 OF 17 MEDLINE on STN DUPLICATE 9

88176029. PubMed ID: 3281092. Constitutive c-myc expression enhances the response of murine **mast cells** to IL-3, but does not eliminate their requirement for growth factors. Hume C R; **Nocka K**

H; Sorrentino V; Lee J S; Fleissner E. (Sloan Kettering Division, Graduate School of Medical Sciences, Cornell University, New York, New York 10021.) Oncogene, (1988 Mar) 2 (3) 223-6. Journal code: 8711562. ISSN: 0950-9232. Pub. country: ENGLAND: United Kingdom. Language: English.

AB An interleukin-3 (IL-3) dependent **mast cell** line (MC) was infected with a recombinant retrovirus expressing the proto-oncogene c-myc and the drug selectable marker neo. Cells containing the transcriptionally activated c-myc **gene** displayed an increased growth rate in liquid culture and a higher cloning efficiency in soft agar when compared to control virus infected cells. All infected cells remained absolutely dependent on IL-3 for growth and were not tumorigenic in nude mice. Similar results were obtained with two additional IL-3 dependent cell lines, the **mast cell** 32D and the pre-B-cell Ea3. Thus, while constitutive expression of c-myc potentiates the response of **mast cells** to IL-3, it is not sufficient to eliminate their requirement for growth factors.

=> s l2 and "MC14"
L5 1 L2 AND "MC14"

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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2002:449849 Document No. 137:32077 Allergic hypersensitivity-associated genes and proteins for diagnosis and treatment of rhinitis, atopic dermatitis, urticaria, asthma and mastocytosis. **Nocka, Karl; Pirozzi, Gregory; Einstein, Richard** (UCB, S.A., Belg.). PCT Int. Appl. WO 2002046389 A2 20020613, 119 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46180 20011207. PRIORITY: US 2000-PV251835 20001208; US 2001-PV275479 20010314; US 2001-PV279115 20010328; US 2001-PV280143 20010402.

AB The invention relates generally to the changes in gene expression in **mast cells** during maturation and in tissues removed from patients with urticaria or allergic hypersensitivity relative to gene expression in **mast cells** removed from normal subjects. The invention specifically relates to four novel gene families which are differentially expressed in **mast cells** and allergic hypersensitivity diseases, such as urticaria, compared to normal tissues. The genes and protein products are useful for diagnosis and treatment of seasonal rhinitis, atopic dermatitis, urticaria, asthma, mastocytosis, and allergic hypersensitivity. The genes and proteins are also useful for identifying agonists and antagonists for therapeutic use.

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Quotation marks (or apostrophes) must be used in pairs, one before and one after the expression you are setting off or masking.

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L6 1 L2 AND "AA447527"

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L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2002:449849 Document No. 137:32077 Allergic hypersensitivity-associated genes and proteins for diagnosis and treatment of rhinitis, atopic dermatitis, urticaria, asthma and mastocytosis. **Nocka, Karl; Pirozzi, Gregory; Einstein, Richard** (UCB, S.A., Belg.).
PCT Int. Appl. WO 2002046389 A2 20020613, 119 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46180 20011207. PRIORITY: US 2000-PV251835 20001208; US 2001-PV275479 20010314; US 2001-PV279115 20010328; US 2001-PV280143 20010402.

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L7 1 L2 AND "AY033593"

=> d l7 cbib abs

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2002:449849 Document No. 137:32077 Allergic hypersensitivity-associated genes and proteins for diagnosis and treatment of rhinitis, atopic dermatitis, urticaria, asthma and mastocytosis. **Nocka, Karl; Pirozzi, Gregory; Einstein, Richard** (UCB, S.A., Belg.).
PCT Int. Appl. WO 2002046389 A2 20020613, 119 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46180 20011207. PRIORITY: US 2000-PV251835 20001208; US 2001-PV275479 20010314; US 2001-PV279115 20010328; US 2001-PV280143 20010402.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.35	58.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.93	-6.93

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